07-21-03

1642

Express Mail Label No.: EL 933534033 US
Date of Deposit: July 18, 2003
Attorney Docket No. 58118 RCE (47992)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS	Samelson, et al.	EXAMINER:	Helms, Larry Ronald
U.S.S.N.:	09/597,920	GROUP:	1642
FILED:	June 19, 2000	Conf. No.	4586
FOR:	THE PROTEIN TYROSINE KINASE SUBSTRATE LAT AND ITS USE IN THE IDENTIFICATION OF (ANT)AGONISTS OF THE KINASE		

****

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service with sufficient postage as Express Mail Label No. EL 933534033 US in an envelope addressed to: Mail Stop Petitions, Atten: Group Director, Art Unit 1642, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on July 18, 2003.

By: Helen Murray Tarbi
Helen Murray Tarbi

****

Mail Stop Petitions
Attn: Technology Center Director
For Group 1642
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PETITION TO WITHDRAW FINALITY OF OFFICE ACTION

This petition is in response to the Final Office Action mailed June 4, 2003. While the cover page of the Office Action states the action is non-final, the final paragraph of the Office Action states that the action is Final. The Office Action was mailed after Applicants filed a Request for Continued Examination (RCE) under 37 CFR § 1.114. In the Office Action, the Examiner indicated that the request was acceptable and that the RCE had been established. A Copy of the Final Office Action is provided as Exhibit A.

Applicants filed the RCE in response to the Examiner's Advisory Action mailed March 7, 2003 in which the Examiner indicated that Applicants' Response filed February 4, 2003 raised new issues that would require further consideration and/or search. A copy of the Advisory Action is attached as Exhibit B. A Copy of the Response filed February 4, 2003 is attached as Exhibit C. Applicants' filed the RCE to obtain entry of Amendments and full consideration of the Response filed February 4, 2003. A copy of Applicants' Amendments and Remarks accompanying the filing of the RCE are provided at Exhibit D. The Amendments and Response were a bona fide attempt to advance the prosecution of the application.

In the Examiner's Final Office Action mailed June 4, 2003. The Examiner indicated the Office Action was made final because Applicants' amendment necessitated new grounds of rejection.

Applicants respectfully submit that the finality of the Office Action is improper. MPEP 706.07(b) which governs the determination of making final a first action after filing an RCE (see MPEP-706.07(h), VIII) provides that it is not proper to make final a first office action in a continuing application, where the material earlier presented in the earlier application was denied entry because (a) new issues were raised requiring further consideration and/ or search or (b) issues of new matter were raised.

In view of the fact that the Finality of the Office Action is improper, Applicants respectfully request reconsideration of this action and withdrawal of the finality of the Office Action.

Applicants believe that no fee is due with this Response. However, please charge any necessary fees required in connection with the papers transmitted herewith to Deposit Account No. 04-1105.

If there are any questions or if any clarification is needed, please do not hesitate to contact Applicants' undersigned attorney.

By: Dianne Rees

Dianne M. Rees, Ph.D. (Reg. 45,281)
EDWARDS & ANGELL, LLP
PO BOX 9169
Boston, Massachusetts 02209
(617) 951-3351

Customer No: 21,874

BOS2_341916.1

Express Mail Label No.: EL 933534033 US
Date of Deposit: July 18, 2003
Attorney Docket No.: 58118 RCE (47992)
U.S.S.N.: 09/597,920

EXHIBIT A

PFC/CCO/DMQ S8118(47[illegible])

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/597,920	06/19/2000	Lawrence E. Samelson	NIH-05065	4586

21874 7590 06/04/2003

EDWARDS & ANGELL, LLP
P.O. BOX 9169
BOSTON, MA 02209

EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	**PAPER NUMBER**
1642	26

DATE MAILED: 06/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

final resp due
Edwards & Angell LLP
101 Federal St. Boston, MA 02110
Docketed For 8/4/03 - 12/4/03
By MM
Approved

appeal due
Edwards & Angell LLP
101 Federal St. Boston, MA 02110
Docketed For 9/4/03 - 12/4/03
By MM
Approved

PTO-90C (Rev. 07-01)

Office Action Summary	Application No.	Applicant(s)	
	09/597,920	SAMELSON ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *61-84* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *61-84* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Request for Continued Examination

1. The request filed on 4/2/03 for a Continued Examination (RCE) under 37 CFR 1.114 based on parent Application No. 09/597,920 is acceptable and a RCE has been established. Claims 61-84 are pending and are currently under prosecution. An action on the RCE follows.

2. Claims 4-6, 29, 33, 37-60 have been cancelled.

Claims 61-84 have been added.

3. Claims 61-84 are under examination.

4. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

5. The following Office Action contains some NEW GROUNDS of rejection .

Rejections Withdrawn

6. The rejection of claim 38 under 35 U.S.C. 112, first paragraph, is withdrawn.

7. The rejection of claims 39-44 under 35 U.S.C. 112, first paragraph, is withdrawn in view of the amendments to the claims

Response to Arguments/ NEW GROUNDS of rejection

8. The rejection of newly added claims 73-77, 79-82, 84 under 35 U.S.C. 102(b) as being anticipated by Buday et al (The Journal of Biological Chemistry 269:9019-9023, 1994, IDS #5) and as evidenced from the specification is maintained.

The response filed 4/2/03 has been carefully considured but is deemed not to be persuasive. The response states that with respect to claims 70-84, Buday's antibody is not generated against a portion of LAT comprising at least about five amino acids and this element must be given weight because the way the antibodies are made does impact the structural properties and the antibody of Buday does not recognize at least 5 amino acids of LAT of SEQ ID NO:4 (see page 7-8 of response). In response to this argument, Buday's antibody would be specific for SEQ ID NO:4. This is explained as follows, because the claims recite that the antibody is generated against a polypeptide comprising any 5 or 20 or residues 31-233 of SEQ ID NO:4 the antibody of Buday would recognizes the phosphotyrosine in SEQ ID NO:4 which can be generated against the entire protein (comprising) or any residues that contain the phosphotyrosine residue. If the entire protein was used as an immunogen or any fragment that has the phosphotyrosine residue, antibodies can be generated that bind the phosphotyrosine residue, such as Buday's. Thus, the art reads on the claims.

9. The rejection of newly added claims 73-78, 80-83 under 35 U.S.C. 102(e) as being anticipated by Hirth et al (U.S. Patent 5,958,959, filed 6/1/95) is maintained.

The response filed 4/2/03 has been carefully considured but is deemed not to be persuasive. The response states that with respect to claims 70-84, Hirth's antibody is not generated against a portion of LAT comprising at least about five amino acids (see page 8 of response). In response to this argument, Hirth's antibody would be specific for SEQ ID NO:4. This is explained as follows, because the claims recite that the antibody is generated against a polypeptide comprising any 5 or 20 or residues 31-233 of SEQ ID NO:4 the antibody of Hirth would recognizes the phosphotyrosine in SEQ ID NO:4 which can be generated against the entire protein (comprising) or any residues that contain the phosphotyrosine residue. If the entire protein was used as an immunogen or any fragment that has the phosphotyrosine residue, antibodies can be generated that bind the phosphotyrosine residue, such as Hirth's. Thus, the art reads on the claims.

Claim Rejections - 35 USC § 112

10. Claims 61-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 61 and 67 have been amended to recite "does not cross-react with other non-LAT ZAP 70 or non-LAT Syk substrates". The response filed 4/2/03 states that support for the limitation can be found at page 38, lines 9-12. The response filed 4/2/03

has bee carefully considured but is deemed not to be persuasive. The specification at the cited location states "the specificity of a LAT fragment for specific binding agents is confirmed by ensuring non-crossreactivity with other ZAP-70 and/or Syk substrates". The specification does not support antibodies that do not cross react with "non-LAT ZAP 70" or "non-LAT Syk substrates" because the specification at the recited page and lines is directed to fragments that have a certain specificity by confirming non crossreactivity to other ZAP-70 and Syk substrates and Lat fragments capable of eliciting antibodies capable of distinguishing LAT from LAT homologs. The specification at the sited place is not directed to antibodies that do not crossreact to non-LAT ZAP 70 or non-LAT Syk substrates. Applicant is required to provide specific support in the application as originally filed or remove the limitation from the claims.

11. Claims 74-77 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 74-77 are indefinite for reciting for example in claim 74 "polypeptide comprising at least five amino acids comprises at least about 20 amino acids" because it is not clear if the polypeptide comprises 5 or 20 amino acids. In addition, claim 75 is indefinite for reciting "comprises at least about five amino acids comprises SEQ ID NO:4" because it is not clear if this claim is further limiting claim 73. claim 76 and 77

are indefinite because again it is unclear if the polypeptide has 5 or 20 residues because of claim 74's indefinite nature.

Conclusion

12. No claim is allowed.

13. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00

am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879

Express Mail Label No.: EL 933534033 US
Date of Deposit: July 18, 2003
Attorney Docket No.: 58118 RCE (47992)
U.S.S.N.: 09/597,920

EXHIBIT B

FC1 CCQ/DMLR 58118(47992)

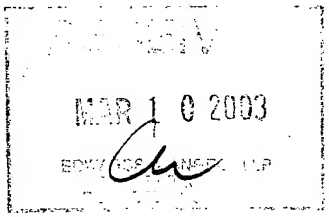
UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/597,920	06/19/2000	Lawrence E. Samelson	NIH-05065	4586

7590 03/07/2003

Peter F. Corless
Edwards & Angell, LLP
P.O. Box 9169
Boston, MA 02209



EXAMINER	
HELMS, LARRY RONALD	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/07/2003

22

Please find below and/or attached an Office communication concerning this application or proceeding.

Appeal Brief Due
Edwards & Angell LLP
Dike, Bronstein, Roberts & Cushman
101 Federal St. Boston, MA 02110
Date Rec'd 3/10/03
Docketed For 4/4/03-5/4/03
By
Approved

PTO-90C (Rev. 07-01)

Advisory Action	Application No.	Applicant(s)	
	09/597,920	SAMELSON ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

--The MAILING DATE of this communication app ars on the cover sh t with the correspondence address --

THE REPLY FILED 04 February 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *04 November 2002*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☒ The proposed amendment(s) will not be entered because:

(a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: *See Continuation Sheet*.

3.☒ Applicant's reply has overcome the following rejection(s): *See Continuation Sheet*.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *see above*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *none*.

Claim(s) objected to: *none*.

Claim(s) rejected: *4-6, 29, 33, 37-44*.

Claim(s) withdrawn from consideration: _____.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

Continuation of 2. NOTE: The newly proposed claim amendments would require a new search because the limitation of does not cross-react with non-LAT ZAP70 or non-syk substrates was not search and amino acids 31-233 of LAT was not searched and claims 61-78 add additional limitations of a portion of 5 amino acids.

Continuation of 3. Applicant's reply has overcome the following rejection(s): IF IF IF entered 112 first for claim 38 and 112 first for claims 39-44 and 102(b) and 102(e).

Express Mail Label No.: EL 933534033 US
Date of Deposit: July 18, 2003
Attorney Docket No.: 58118 RCE (47992)
U.S.S.N.: 09/597,920

EXHIBIT C

PFC/CCO/Dmr

5

Mailing Date:	02/04/03	Attorney/Sec:	PFC/dmr
Client:	NIH (47992)	Docket No.:	58118
Inventors:	Samelson et al.		
Serial No.:	09/597,920	Patent No.:	
Filing Date:	06/19/00	Grant Date:	

The dating stamp of the Patent and Trademark Office hereon will be taken as the date of filing of:

Amendment or Response After Final Rejection - Transmittal; Amendment and Response To Final Office Action; and check in the amount of $110.00 to cover the fee.

Due Date: February 8, 2003

Practitioner's Docket No. 47992/58118 (formerly NIH-05065) *PATENT*

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Samelson et al.

Serial No.: 09/597,920 Group No.: 1642

Filed: June 19, 2000 Examiner: Helms, Larry Ronald

For: THE PROTEIN TYROSINE KINASE SUBSTRATE LAT AND ITS USE IN THE IDENTIFICATION OF (ANT)AGONISTS OF THE KINASE

Box AF
Assistant Commissioner for Patents
Washington, D.C. 20231

RESPONSE UNDER 37 C.F.R. 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP
1642

NOTE: To take advantage of the expedited procedure the envelope in which this paper is mailed must be addressed as shown and must also be marked "Box AF" in the lower left hand corner. Alternatively, this paper can be hand carried to the particular Examining Group or other area of the Office in which the application is pending, in which case any envelope in which this paper is placed must be marked as in the bold type box above. Notice of Sept. 20, 1985 (1059 O.G. 19-20).

AMENDMENT OR RESPONSE AFTER FINAL REJECTION—TRANSMITTAL

1. Transmitted herewith is an amendment after final rejection (37 C.F.R. 1.116) for this application.

CERTIFICATION UNDER 37 C.F.R. 1.8(a) and 1.10*
*(When using Express Mail, the Express Mail label number is **mandatory**; Express Mail certification is optional.)*

I hereby certify that, on the date shown below, this correspondence is being:

MAILING

☒ deposited with the United States Postal Service in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

37 C.F.R. 1.8(a)

☐ with sufficient postage as first class mail.

37 C.F.R. 1.10*

☒ as "Express Mail Post Office to Address" Mailing Label No. EF394616843US **(mandatory)**

TRANSMISSION

☐ transmitted by facsimile to the Patent and Trademark Office.

Deanna M. Rivernider
Signature

Date: 2/4/03

Deanna M. Rivernider
(type or print name of person certifying)

***WARNING:** *Each paper or fee filed by "Express Mail" must have the number of the "Express Mail" mailing label placed thereon prior to mailing. 37 C.F.R. 1.10(b).*
"Since the filing of correspondence under § 1.10 without the Express Mail mailing label thereon is an oversight that can be avoided by the exercise of reasonable care, requests for waiver of this requirement will not be granted on petition." Notice of Oct. 24, 1996, 60 Fed. Reg. 56,439, at 56,442.

NOTE: *Response to Final Rejection—Avoiding Extension Fees "In patent applications wherein a three month Shortened Statutory Period (SSP) is set for response to a Final Rejection, the response would best be filed within two months of the date of the Office Action, If filed within two months, any Advisory Action mailed after the SSP expires will reset the SSP to expire on the date of the Advisory Action for extension fee purposes, but never more than six months from the date of the Final Rejection." Notice of Nov. 30, 1990 (1122 O.G. 571 to 591).*

STATUS

2. Applicant is

[ ] a small entity. A statement:

[ ] is attached.

[ ] was already filed.

[X] other than a small entity.

EXTENSION OF TERM

NOTE: *As to a Supplemental Amendment filed in response to a final office action, the Notice of December 10, 1985 (1061 O.G. 34-35) states:*

> *"If a timely response has been filed after a Final Office Action, an extension of time is required to permit filing and/or entry of a Notice of Appeal or filing and/or entry of an additional amendment after expiration of the shortened statutory period unless the timely-filed response placed the application in condition for allowance. Of course, if a Notice of Appeal has been filed within the shortened statutory period, the period has ceased to run."*

3. *(complete (a) or (b), as applicable)*

(a) [ ] Applicant petitions for an extension of time under 37 C.F.R. 1.136 (fees: 37 C.F.R. 1.17(a)(1)-(4)) for the total number of months checked below:

	Extension (months)	Fee for other than small entity	Fee for small entity
[X]	one month	$ 110.00	$ 55.00
[ ]	two months	$ 390.00	$ 195.00
[ ]	three months	$ 890.00	$ 445.00
[ ]	four months	$1,390.00	$ 695.00

Fee: $ 110.00

If additional extension of time is required, please consider this a petition therefor.

(check and complete the next item, if applicable)

[ ] An extension for _____ months has already been secured and the fee paid therefor of $ _____ is deducted from the total fee due for the total months of extension now requested.

Extension fee due with this request $ 110.00

OR

(b) [ ] Applicant believes that no extension of term is required. However, this conditional petition is being made to provide for the possibility that applicant has inadvertently overlooked the need for a petition and fee for extension of time.

FEE FOR CLAIMS

4. The fee for claims (37 C.F.R. 1.16(b)-(d)) has been calculated as shown below:

					SMALL ENTITY			OTHER THAN A SMALL ENTITY	
	Claims Remaining After Amendment		Highest No. Previously Paid For	Present Extra	Rate	Addit. Fee	*OR*	Rate	Addit. Fee
Total	*	Minus	**	=	x $9 =	$		x $18 =	$
Indep.	*	Minus	***	=	x $40 =	$		x $80 =	$
[ ] First Presentation of Multiple Dependent Claim					+ $135 =	$		+ $270 =	$
					Total Addit. Fee	$_____	*OR*	Total Addit. Fee	$_____

* If the entry in Col. 1 is less than the entry in Col. 2, write "O" in Col. 3,

** If the "Highest No. Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest No. Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest No. Previously Paid For" (Total or Indep.) is the highest number found in the appropriate box in Col. 1 of a prior amendment or the number of claims originally filed.

WARNING: *See 37 C.F.R. § 1.116.*

(complete (c) or (d), as applicable)

(c) [X] No additional fee is required.

OR

(d) [ ] Total additional fee required is $ _____.

FEE PAYMENT

5. [X] Attached is a check in the sum of $ 100.00.

[ ] Charge Account No. _____ the sum of $ _____.
A duplicate of this transmittal is attached.

FEE DEFICIENCY

NOTE: Where there is a fee deficiency and there is no authorization to charge an account, additional fees are necessary to cover the additional time consumed in making up the original deficiency. If the maximum, six-month period has expired before the deficiency is noted and corrected, the application is held abandoned. In those instances where authorization to charge is included, processing delays are encountered in returning the papers to the PTO Finance Branch in order to apply these charges prior to action on the case. Authorization to charge the deposit account for any fee deficiency should be checked. See the Notice of April 7, 1986, (1065 O.G. 31-33).

6. [X] If any additional extension and/or fee is required, charge Account No. 04-1105 .

AND/OR

[X] If any additional fee for claims is required, charge Account No. 04-1105 .

SIGNATURE OF PRACTITIONER

Reg. No. 33,860

Peter F. Corless
(type or print name of practitioner)

Tel. No. (617) 523-6440

EDWARDS & ANGELL, LLP
Dike, Bronstein, Roberts & Cushman, IP Group
P.O. Box 9169
P.O. Address
Boston, Massachusetts 02209

Attorney Docket No. 47992/58118 (formerly NIH-05065)
Express Mail Label No.: EF394616843US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS	Samelson, et al.	EXAMINER:	Helms, Larry Ronald
U.S.S.N.:	09/597,920	GROUP:	1642
FILED:	June 19, 2000	Conf. No.	4586
FOR:	THE PROTEIN TYROSINE KINASE SUBSTRATE LAT AND ITS USE IN THE IDENTIFICATION OF (ANT)AGONISTS OF THE KINASE		

RESPONSE UNDER 37 C.F.R. § 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP 1642

BOX AF
Commissioner for Patents
Washington, D.C. 20231

AMENDMENT AND RESPONSE TO FINAL OFFICE ACTION

Sir:

This paper is responsive to the Final Office Action mailed August 8, 2002 and to the Advisory Action mailed October 28, 2002.

AMENDMENT

In the Specification

At page 10, after line 13, please **insert** the following:

--FIGURE 17 is a schematic diagram illustrating the role of LAT in linking the TCR to cellular activation.

FIGURE 18 is a schematic diagram showing the structure of the plasmid pEF BOS. The boxes indicate the SV40 origin, human EI-1α promoter region, the stuffer sequence from

CDM8 and poly(A) adenylation site, respectively. The slashed areas in the EF-1α promoter region represent sequences from the first exon and part of the second exon, respectively. The lines flanking the boxes are sequences from pUC119. Major recognition sites for restriction enzymes are shown.--

Please **delete** pages 37 and 60, and renumber the remaining pages as appropriate.

In the Claims

Please **cancel** claims **40** and **42-60**.

Please **add** claims **61-78**.

Please **amend** claim **4, 39** and **41**.

4. (Amended) A purified antibody which is generated against a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 and which specifically binds to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4, but which does not cross-react with non-LAT ZAP 70 or non-LAT Syk substrates.

39. (Amended) The purified antibody of any of Claims 4-6, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises the cytostolic tail of LAT.

41. (Amended) The purified antibody of any of Claims 4-6, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises amino acids 31-233 of LAT.

61. (New) A purified antibody which is generated against a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4, wherein the at least a portion of the amino acid sequence comprises a phosphotyrosine residue and wherein the antibody specifically binds to a phosphorylated LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4, but which does not cross-react with other non-LAT ZAP 70 or non-LAT Syk substrates.

62. (New) The purified antibody of Claim 61, wherein the at least a portion comprises at least about 5 amino acids of SEQ ID NO. 4.

63. (New) The purified antibody of Claim 61, wherein the at least a portion comprises at least about 20 amino acids of SEQ ID NO. 4.

64. (New) The purified antibody of Claim 61, wherein the at least a portion comprises of SEQ ID NO. 4.

65. (New) The purified antibody of any of Claims 61-64, wherein the antibody is a polyclonal antibody.

66. (New) The purified antibody of any of Claims 61-64, wherein the antibody is a monoclonal antibody.

67. (New) A purified antibody which is generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4 and which specifically binds to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4.

68. (New) The purified antibody of Claim 67, wherein the polypeptide comprising at least about five amino acids comprises at least about 20 amino acids of SEQ ID NO: 4.

69. (New) The purified antibody of Claim 67, wherein the polypeptide comprising at least about five amino acids comprises SEQ ID NO: 4.

70. (New) The purified antibody of Claim 68, wherein said polypeptide comprising at least about twenty amino acids of the amino acid sequence of SEQ ID NO: 4 comprises the cytostolic tail of LAT.

71. (New) The purified antibody of Claims 70, wherein said polypeptide comprising at least about twenty amino acids of the amino acid sequence of SEQ ID NO: 4 comprises amino acids 31-233 of LAT.

72. (New) The purified antibody of any of Claims 67-71, wherein the antibody is a polyclonal antibody.

73. (New) The purified antibody of any of Claims 67-71, wherein the antibody is a monoclonal antibody.

74. (New) A purified antibody which is generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4, wherein the at least about five amino acids comprises a phosphotyrosine residue and wherein the antibody specifically binds to a phosphorylated LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4.

75. (New) The purified antibody of claim 74, wherein the polypeptide comprising at least about five amino acids comprises at least about 20 amino acids of SEQ ID NO: 4.

76. (New) The purified antibody of claim 74, wherein the polypeptide comprising at least about five amino acids comprises SEQ ID NO: 4.

77. (New) The purified antibody of any of Claims 74-76, wherein the antibody is a polyclonal antibody.

78. (New) The purified antibody of any of Claims 74-76, wherein the antibody is a monoclonal antibody.

RESPONSE

Pending claims

Claims 4-6, 29, 33 and 37-60 are pending. Claims 45-60 are withdrawn from consideration. Upon entry of this Amendment and Response, claims 4-6, 29, 33, 37- 39, 41 and 61-78 are presented for consideration. A clean copy of claims 4-6, 29, 33, 37- 39, 41 and 61-78 is provided for the Examiner's convenience.

Claims are canceled herein solely to expedite prosecution of the instant application and without prejudice to pursuing these claims in continuing and other related applications. No new matter is added by this amendment. Support for amended claims 4, 39 and 41 and newly added claims 61-78 are found throughout the specification, in the claims as originally presented and in the Figures. In particular, attention is directed to the present application at page 38, page 41, lines 3-8, page 40, line 25 through page 41, line 1, and page 57, lines 5-7. Support for antibodies which do not cross-react with non-LAT ZAP 70 or non-LAT Syk substrates may be found at least at page 38, lines 9-12. Support for antibodies that are generated against a polypeptide of at least about 5 amino acids of the amino acid sequence of SEQ ID NO. 4 may be found at page 44, lines 6-9, for example.

It is submitted that the amendments and newly added claims may be properly entered at this time, i.e., after final rejection, pursuant to 37 CFR §1.116, because the amendments do not raise any new issues or require a new search, and they reduce issues for appeal. Additionally, a number of claims have been cancelled.

Applicants thank the Examiner for his helpful comments during the telephonic interview of October 24, 2002. The amendments and newly added claims provided with this response are made to address the issues raised by the Examiner during the interview. It is believed that the amendments and newly added claims place the application in condition for allowance. Accordingly, entry of the amendments and newly added claims is earnestly solicited at this time.

Objection to the Specification

The Examiner has objected to the Specification and states that "Schematic A" provided on page 37 should be removed and provided in the form of a Figure.

Applicants provided with their previous Amendment and Response to Final Rejection new Figures 17 and 18, to provide formal drawings corresponding to Schematic A and B respectively and have amended the Brief Description of the Drawings and the specification, as appropriate, to reflect this change.

Applicants thank the Examiner for approving the drawings submitted with Applicants' previous Response filed October 8, 2002, as indicated by the Advisory Action mailed October 28, 2002. Applicants respectfully request entry of the amendments to the Specification to describe the newly added Figures.

Rejection of Claims 4, 6, 29 and 37 Under 35 U.S.C. § 102(b) (Buday)

Claims 4, 6, 29 and 37 are rejected under 35 U.S.C. § 102(b) as being anticipated by Buday, et al., *The Journal of Biological Chemistry* 269: 9019-9023, 1994 ("Buday").

The Examiner asserts that Buday teaches an antibody specific for phosphotyrosine which is a portion of SEQ ID NO. 4 and therefore that the antibody of Buday would bind to SEQ ID NO: 4.

Applicants respectfully traverse the rejection as it would be applied to the amended and newly added claims. As amended, claims 4-6, 29, 33, 37- 39, 41 and 61-66 recite antibodies that specifically bind to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4 and do not cross-react with non-LAT ZAP 70 or non-LAT Syk substrates. Claims 67-78 recite that the antibodies are generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4 and that specifically bind to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4.

Unlike the antibodies of claims 4-6, 29, 33, 37- 39, 41 and 61-66, Buday's antibody *would* cross react with non-LAT ZAP 70 or non-LAT Syk substrates, since it would react non-specifically with *any* polypeptides comprising a phosphotyrosine group. Therefore Buday neither teaches nor suggests the antibodies of claims 4-6, 29, 33, 37- 39, 41 and 61-66.

With respect to claims 67-78, Buday's antibody is *not* generated against a portion of a LAT polypeptide comprising *at least about five amino acids of SEQ ID NO. 4*. This element of claims 67-78 must be given weight because the way in which the claimed antibodies are made *does* impact the structure and properties of the antibodies. The antigen-binding site of the claimed antibodies must recognize at least 5 amino acids of SEQ ID NO. 4 and must specifically

bind to a LAT polypeptide according to SEQ ID NO. 4 (i.e., the full length LAT polypeptide). There is no teaching or suggestion of antibodies with these properties anywhere in Buday. To the extent Buday's antibody might arguably recognize a phosphorylated tyrosine in a phosphorylated LAT polypeptide, it does not recognize a sequence of at least 5 amino acids of a LAT polypeptide according to SEQ ID NO: 4 and therefore does not have the same binding specificity required by claims 67-78.

Therefore, because Buday does not teach each element of the claims as required under 35 U.S.C. § 102, Buday does not anticipate the claims. See *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978) ("[r]ejections under 35 U.S.C. §102 are proper only when the claimed subject matter is identically disclosed or described in the prior art.").

Applicants respectfully request that in view of the above arguments, the rejection should be reconsidered and withdrawn.

Rejection of Claims 4-5, 29 and 33 Under 35 U.S.C. § 102(e) (Hirth)

Claims 4-5, 29 and 33 stand rejected under 35 U.S.C. § 102(e) over Hirth, et al., U.S. Patent 5,058,959 ("Hirth"). The Examiner asserts that the antibody of Hirth is directed against a phosphotyrosine residue and as such, because the term "portion" reads on a single amino acid, Hirth allegedly anticipates the claims.

Applicants respectfully traverse the rejection as applied to the amended and newly added claims. As discussed above, as amended, claims 4-6, 29, 33, 37- 39, 41 and 61-66 require that the antibodies recognize and *specifically* bind to a LAT polypeptide according to SEQ ID NO: 4 (i.e., a full length LAT polypeptide) and must *not cross react* with non-LAT ZAP 70 or non-LAT Syk substrates (i.e., non-LAT polypeptides which are phosphorylated by ZAP 70 and/or Syk).

Hirth's antibodies would non-specifically cross-react with any polypeptides comprising a phosphotyrosine, including non-LAT ZAP 70 or non-LAT Syk substrates. Additionally, Hirth neither teaches nor suggests antibodies which recognize and specifically bind to a full length LAT polypeptide according to SEQ ID NO: 4 and which are generated against a polypeptide which comprises at least about 5 amino acids of SEQ ID NO. 4 as claimed in claims 67-78. Hirth nowhere teaches or suggests antibodies with these properties.

Therefore, in view of the above arguments, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejection of Claim 38 Under 35 U.S.C. § 112, First Paragraph

Claim 38 is rejected under 35 U.S.C.§ 112, first paragraph. The Office Action expressly acknowledges that the specification is enabling for an antibody that binds a portion of SEQ ID NO:4. However, the position is taken that the specification does not reasonably enable an antibody that binds to "just any 20 amino acids" of SEQ ID NO:4 because antibodies generated against 20 amino acid fragments would not recognize the folded protein and as such would not be useful in detection. The Examiner concludes that it would require undue experimentation to use the claimed invention.

Applicants respectfully traverse the rejection. Antibodies are routinely generated against protein fragments and are routinely used in assays which do not rely on detecting tertiary conformations of proteins. For example, it was standard in the art at the time of filing (and still is) to perform Western blots of proteins electrophoresed on polyacrylamide gels comprising 10% SDS. In such gels, the proteins are denatured and do not retain the tertiary structure of the native protein. Yet Western blots have undeniable utility in assays which rely on the detection of specific proteins (e.g., such as in diagnostic assays). Additionally, antibodies generated against

LAT peptides are also able to recognize non-denatured proteins in Flow Cytometry Assays as well as in immunohistochemistry assays. Accordingly, Applicants respectfully submit that the rejection of claim 38 is improper and should be reconsidered and withdrawn.

Rejection of Claims 39-44 Under 35 U.S.C. § 112, First Paragraph

Claims 39-44 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) , at the time the application was filed, had possession of the claimed invention. The Examiner specifically objects to claims which recite "wherein SEQ ID NO: 4 comprises a carboxy-terminus and an amino-terminus, wherein said portion comprises at least 20 amino acids from" either the amino-terminus or carboxy-terminus. The Examiner asserts that "there is no support for antibodies that bind to at least 20 amino acids from the amino-terminal or carboxy-terminal."

Applicants respectfully submit that the rejection is moot in view of the deletion of the objected to language in the claims and traverse the rejection. Amended claim 39 recites that the polypeptide against which the antibodies are generated comprises the cytostolic tail of LAT. Support for this claim language may be found in the present application at page 40, line 25 through page 41, line 1. Amended claim 41 recites that the polypeptide against which the antibodies are generated comprises amino acids 31 to 233 of LAT. Support for the latter claim language may be found at least at page 57, lines 5-7. This sequence represents the sequence used as an immunogen to generate the antibodies disclosed in Applicants' Examples.

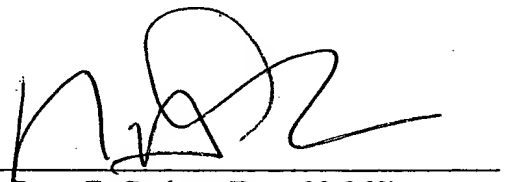
These amendments are made solely to expedite the prosecution of the instant application as Applicants respectfully submit that specification clearly states at page 40 that that the present invention is not limited to specific portions of LAT for the generation of antibodies. As such, claim 4 includes antibodies which recognize both N- and C-termini, as well as internal fragments of LAT and mutant forms of LAT.

In view of the above amendments and arguments, Applicants respectfully request that the rejection be reconsidered and withdrawn.

CONCLUSION

Applicants submit that the claims are allowable and that the Application is now in condition for allowance. Applicants respectfully request early favorable action by the Examiner.

If the Examiner believes that a telephone conversation with Applicants' agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned agent of record.

By: 

Peter F. Corless (Reg. 33,860)
Dianne Rees, Ph.D. (Reg. 45,281)
EDWARDS & ANGELL, LLP
PO BOX 9169
Boston, Massachusetts 02209
(617) 951-3351

Customer No: 21,874

Marked-Up Version of Claims Showing Changes Being Made

4. A purified antibody which is generated against a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 and which specifically binds to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4, but which does not cross-react with other non-LAT ZAP 70 or non-LAT Syk substrates.

39. (Amended) The purified antibody of any of Claims [Claim] 4-6, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises the cytostolic tail of LAT [wherein SEQ ID NO: 4 comprises a carboxy-terminus and an amino terminus, wherein said portion comprises at least 20 amino acids from the carboxy-terminus].

41. (Amended) The purified antibody of any of Claims [Claim 5] 4-6, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises amino acids 31-233 of LAT [wherein SEQ ID NO: 4 comprises a carboxy-terminus and an amino- terminus, wherein said portion comprises at least 20 amino acids from the carboxy-terminus].

Attorney Docket No. 47992/58118 (formerly NIH-05065)
U.S.S.N.: 09/597,920
Filed: June 19, 2000.

PENDING CLAIMS UPON ENTRY OF AMENDMENT

4. (Amended) A purified antibody which is generated against a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 and which specifically binds to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4, but which does not cross-react with other non-LAT ZAP 70 or non-LAT Syk substrates.

5. A purified antibody of Claim 4, wherein said antibody is a polyclonal antibody.

6. The purified antibody of Claim 4, wherein said antibody is a monoclonal antibody.

29. The purified antibody of claim 4, wherein said antibody is directed against SEQ ID NO:4.

33. The purified antibody of claim 5, wherein the antibody is directed against SEQ ID NO: 4.

37. The purified antibody of Claim 6, wherein said antibody is directed against SEQ ID NO:4.

38. The purified antibody of Claim 4, wherein said portion comprises at least 20 amino acids of SEQ ID NO: 4.

39. (Amended) The purified antibody of any of Claims 4-6, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises the

cytostolic tail of LAT.

41. (Amended) The purified antibody of any of Claims 4-6, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises amino acids 31-233 of LAT.

61. (New) A purified antibody which is generated against a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4, wherein the at least a portion of the amino acid sequence comprises a phosphotyrosine residue and wherein the antibody specifically binds to a phosphorylated LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4, but which does not cross-react with other non-LAT ZAP 70 or non-LAT Syk substrates.

62. (New) The purified antibody of Claim 61, wherein the at least a portion comprises at least about 5 amino acids of SEQ ID NO. 4.

63. (New) The purified antibody of Claim 61, wherein the at least a portion comprises at least about 20 amino acids of SEQ ID NO. 4.

64. (New) The purified antibody of Claim 61, wherein the at least a portion comprises of SEQ ID NO. 4.

65. (New) The purified antibody of any of Claims 61-64, wherein the antibody is a polyclonal antibody.

66. (New) The purified antibody of any of Claims 61-64, wherein the antibody is a monoclonal antibody.

67. (New) A purified antibody which is generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4 and which specifically binds to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4.

68. (New) The purified antibody of Claim 67, wherein the polypeptide comprising at least about five amino acids comprises at least about 20 amino acids of SEQ ID NO: 4.

69. (New) The purified antibody of Claim 67, wherein the polypeptide comprising at least about five amino acids comprises SEQ ID NO: 4.

70. (New) The purified antibody of Claim 68, wherein said polypeptide comprising at least about twenty amino acids of the amino acid sequence of SEQ ID NO: 4 comprises the cytostolic tail of LAT.

71. (New) The purified antibody of Claims 70, wherein said polypeptide comprising at least about twenty amino acids of the amino acid sequence of SEQ ID NO: 4 comprises amino acids 31-233 of LAT.

72. (New) The purified antibody of any of Claims 67-71, wherein the antibody is a polyclonal antibody.

73. (New) The purified antibody of any of Claims 67-71, wherein the antibody is a monoclonal antibody.

74. (New) A purified antibody which is generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4, wherein the at least about five amino acids comprises a phosphotyrosine residue and wherein the antibody

specifically binds to a phosphorylated LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4.

75. (New) The purified antibody of claim 74, wherein the polypeptide comprising at least about five amino acids comprises at least about 20 amino acids of SEQ ID NO: 4.

76. (New) The purified antibody of claim 74, wherein the polypeptide comprising at least about five amino acids comprises SEQ ID NO: 4.

77. (New) The purified antibody of any of Claims 74-76, wherein the antibody is a polyclonal antibody.

78. (New) The purified antibody of any of Claims 74-76, wherein the antibody is a monoclonal antibody.

Express Mail Label No.: EL 933534033 US
Date of Deposit: July 18, 2003
Attorney Docket No.: 58118 RCE (47992)
U.S.S.N.: 09/597,920

EXHIBIT D

pre/cc/Dmr

58118 (47992)

Mailing Date:	4/16/2003	Attorney/Sec:	DMR/hmt
Client:	47992	~~Docket~~ No.:	58118 RCE
Inventors:	Samelson		
Serial No.:	09/597,920	Patent No.:	
Filing Date:	6/19/2000	Grant Date:	

The dating stamp of the Patent and Trademark Office hereon will be taken as the date of filing of:

Copy of Request for Continued Examination filed on April 2, 2003
Copy of post card receipt for same acknowledging receipt on April 2, 2003
Copies of invoices of checks for $820.00 and $750.00 filed with RCE on April 2, 2003
Copy of Amendment and Remarks filed on April 2, 2003
Remarks (included in this paper); and return receipt postcard

Due Date:

Express Mail EL945989385

Attorn y Dock t No. 58118 RCE (47992)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS	Samelson, et al.	EXAMINER:	Helms, Larry Ronald
U.S.S.N.:	09/597,920	GROUP:	1642
FILED:	June 19, 2000	Conf. No.	4586
FOR:	THE PROTEIN TYROSINE KINASE SUBSTRATE LAT AND ITS USE IN THE IDENTIFICATION OF (ANT)AGONISTS OF THE KINASE		

****

CERTIFICATE UNDER 37 C.F.R. § 1.10

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service in an envelope as "Express Mail Post Office to Addressee," mailing label EL945989385US: **BOX RCE**, Commissioner for Patents, Washington, D.C. 20231 on April 16, 2003.

By: Helen Murray Tarbi

Helen Murray Tarbi

****

BOX RCE
Commissioner for Patents
Washington, D.C. 20231

Sir/Madam:

TRANSMITTAL

Enclosed herewith for filing in the subject application are the following:

1. Copy of Request For Continued Examination (RCE) filed on April 2, 2003;
2. Copy of post card receipt for same acknowledging receipt on April 2, 2003;
3. Copies of Invoices of Checks for $820.00 and $750.00 filed with RCE on April 2, 2003;
4. Copy of Amendment and Remarks filed on April 2, 2003;
5. Remarks (included in this paper); and
5. A return receipt postcard.

REMARKS

Applicants submit herewith a copy of their filing of a Request for Continued Examination (RCE) filed on April 2, 2003 and related papers that were inadvertently addressed to BOX REISSUE rather than BOX RCE. Although Applicants believe that no fee is due with this communication, if for any reason, a fee paid is owed, you are hereby authorized and requested to charge Deposit Account No. **04-1105**.

Respectfully submitted,

Date: April 16, 2003

Dianne M. Rees, Ph.D.
(Reg. No. 45,281)
EDWARDS & ANGELL, LLP
P.O. Box 9169
Boston, MA 02209

Telephone: 617-439-4444
Customer No. 21874

EXPRESS MAIL No. EL945938545
Date of deposit of copy of 4/2/03 filing
April 2, 2003

COPY

Attorney Docket No. 58118 RCE (47992)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT(S):	Samelson, et al.		
SERIAL NO:	09/597,920	EXAMINER:	HELMS, Larry Ronald
FILED:	June 19, 2000	GROUP ART NO:	1642
FOR:	THE PROTEIN TYROSINE KINASE SUBSTRATE LAT AND ITS USE IN THE IDENTIFICATION OF (ANT)AGONISTS OF THE KINASE		

CERTIFICATION UNDER 37 C.F.R. 1.10*
*(Express Mail label number is **mandatory**.)*

I hereby certify that this correspondence and the documents referred to as attached herein are being deposited with the United States Postal Service on this date **April 2, 2003** in an envelope as "Express Mail Post Office to Addressee," mailing Label Number **EL932685394 US** addressed to the: Commissioner for Patents, Washington, D.C. 20231.

Helen Murray Tarbi
(type or print name of person mailing paper)

Signature of person mailing paper

BOX ~~REISSUE~~ RCE DMR 4/16/03
Commissioner for Patents
Washington, D.C. 20231

REQUEST FOR CONTINUED EXAMINATION (RCE)
(37 C.F.R. 1.114)

1. Applicant hereby requests continued examination, in accordance with 37 C.F.R. Section 1.114, for the above identified application.

WARNING: *35 U.S.C. 132(b) and Section 1.114 provide for the continued examination of an application and **not** examination of a continuing application). Accordingly, the Office will not permit an applicant to obtain continued examination on the basis of claims that are independent and distinct from the claims previously claimed and examined. Notice of March 10, 2000, 65 Fed Reg 14865, at 14868.*

WARNING: *A continued examination request **cannot** be made if at least one office action under 35 U.S.C. 132 or a notice of allowance under 35 U.S.C. 161 has not been mailed. The provisions of 37 C.F.R. 1.114 also do not apply (1) to a provisional application, an application for a utility or plant patent filed under 35 U.S.C. 111(a); (2) an international application filed under 35 U.S.C. 363 before June 8, 1995; (3) a patent under reexamination; or (4) an application for a design patent. 37 C.F.R. Section 1.114(d).*

NOTE: There is no limit to the number of times the fee for continued examination may be submitted. Notice of March 10, 2000, 65 Fed Reg 14865, at 14868.

*NOTE: Unlike a continuation application, a continued examination request **can** utilize the mailing procedure of 37 C.F.R. 1.8. See 37 C.F.R. Section 1.8(a)(2)(i)(A).*

TIME REQUEST IS BEING MADE

2. This request is being submitted *(check appropriate item(s) below)*:

i. [X] Prior to abandonment of the application

ii. [ ] Payment of the issue fee
- [ ] Prior to payment of issue fee
- [ ] Issue fee has been paid but a petition under Section 1.313 has been granted

iii. [ ] Prior to a decision on appeal to the Board of Patent Appeals & Interferences
- [ ] A notice is being separately sent to the Board of Patent Appeals & Interferences that this Request for Continued Examination is being filed.

NOTE: If such a notice is not sent to the Board, they may refuse to vacate a decision rendered after the filing of the RCE but before recognition by the Office of the RCE request under Section 1.114.

iv. [ ] Appeal to the U.S. Court of Appeals of the Federal Circuit under 35 U.S.C. 14
or [ ] Commencement of a civil action under 35 U.S.C. 146
- [ ] Prior to the filing of such appeal or commencement of civil action
- [ ] Such appeal or commencement of civil action has been terminated

ENCLOSURES

3. Enclosed herewith is/are:

WARNING: If reply to a final or non-final Office action under 35 U.S.C. 132 is outstanding, the submission must meet the reply requirements of Section 1.111. 37 C.F.R. Section 1.114(b).

[ ] An information disclosure statement (37 C.F.R. Section 1.98)
- [ ] Form PTO-1449 (PTO/SB/08A and 08B)

[X] An amendment – **Please enter the Amendment and Remarks filed Herewith.**

[X] New arguments – **(relating to the amendment and previously presented in Applicants' response to the Advisory Action).**

[ ] New evidence in support of patentability

[ ] Other:

FEE FOR REQUEST (37 C.F.R. Section 1.17(e)).

4. This application is on behalf of:

[ ]	Small entity (and status is still as small entity)	$
[X]	Other than a small entity	$ 750.00

Continued Prosecution Request Fee $ 750.00

FEE FOR CLAIMS

NOTE: "The fee for continued examination under Section 1.114 (Section 1.17(e)) does not include additional claims fee (cf. 1.53 (d)(3)(ii))." See Notice of March 10, 2000, 65 Fed Reg 14865, at 14868.

37 C.F.R. 1.53(d)(3) : "The filing fee for a continued prosecution application filed under this paragraph is:

(i) The basic filing fee as set forth in Section 1.16; and

(ii) Any additional Section 1.16 fee due based on the number of claims remaining in the application after entry of any amendment accompanying the request for an application under this paragraph and entry of any amendments under Section 1.116 unentered in the prior application which applicant has requested to be entered in the continued prosecution application."

5. The fee for claims (37 C.F.R. Section 1.16(b)-(d)) has been calculated as shown below:

(Col.1)		(Col. 2)	(Col. 3)	SMALL ENTITY			OTHER THAN A SMALL ENTITY	
Claims Remaining After Amendment		Highest No. Previously Paid For	Present Extra	Rate	Addit. Fee	*OR*	Rate	Addit. Fee
Total	Minus	20	= 0	x $9 =	$		x $18 =	$0.00
Indep.	Minus	3	= 0	x $42 =	$		x $84 =	$0.00
[ ] First Presentation of Multiple Dependent Claim				+ $140 =	$		+ $280 =	$
		Total Addit Fee			$_____	*OR*	**Total Addit. Fee**	$0.00

* If the entry in Col. 1 is less than the entry in Col. 2, write "0" in Col. 3,

** If the "Highest No. Previously Paid For" IN THIS SPACE is less than 20, enter "20".

*** If the "Highest No. Previously Paid For" IN THIS SPACE is less than 3, enter "3".

The "Highest No. Previously Paid For" (Total or Indep.) is the highest number found in the appropriate box in Col. 1 of a prior amendment or the number of claims originally filed.

WARNING: See 37 C.F.R. Section 1.116.

(complete (c) or (d), as applicable)

(c) [X] No additional fee is required.

OR

(d) [ ] Total additional fee required is $0.00

EXTENSION OF TIME

(If an extension of time is appropriate complete (a) or (b), as applicable)

6. The proceedings herein are for a patent application, and the provisions of 37 C.F.R. Section 1.136(a) apply.

(a) [X] Applicant petitions for an extension of time, the fees for which are set out in 37 C.F.R. Section 1.17(a)(1)-(4), for the total number of months checked below:

Extension for (months)	Fee for small entity	Fee for other than small entity
[ ] one month	$ 55	$110
[ ] two months	$ 205	$410
[X] three months	$ 465	$930
[ ] four months	$ 725	$1,450

If an additional extension of time is required, please consider this a petition therefor.

(check and complete the next item, if applicable)

[X] An extension for one month has already been secured, and the fee paid therefor of $110.00 is deducted from the total fee due for the total months of extension now requested.

Extension fee due with this request **$ 820.00**

OR

(b) [ ] Applicant believes that no extension of time is required. However, this is a conditional petition and authorization to pay the necessary fees to provide for the possibility that applicant has inadvertently overlooked the need for a petition and fee for extension of time.

TOTAL FEE(S) DUE

WARNING: *The fee for continued examination under Section 1.114 may not be deferred. 37 C.F.R. Section 1.53(f).*

7. The total fee(s) due is/are:

Continued Prosecution Fee (Section 1.17(e))	$ 750.00
Fee(s) for additional claims (if any) (Section 1.16(b)-(d))	$ 0.00
Extension of time fee (if any) (Section 1.17(a)(1)-(4))	$ 820.00
Total Fee(s) Due:	**$ 1,570.00**

PAYMENT OF FEE(S) DUE

8. Please pay the fee(s) for this continued examination application as follows:

[X] Checks in the amount of $750.00 to cover filing fee and $820.00 to cover the petition for extension of time **$ 1,570.00**

[ ] Charge Account _____ the sum of $ _____

[ ] Charge Credit Card the sum of $ _____
(Credit Card Payment Form (PTO-2038) attached.)

Please charge any required additional fee(s) for Section 1.17(e), Section 1.16(b)-(d) and/or Section 1.17(a)(1)-(4) to

[X] Account 04-1105

[ ] Credit Card (Credit Card Payment Form (PTO-2038) attached.)

INVENTORSHIP

NOTE: *Any change of inventors must be via the procedure set forth in 37 C.F.R. Section 1.48. See Notice of March 10, 2000, 65 Fed Reg 14865, at 14868.*

9. This application as amended names as inventors:

[X] the same inventors as previously designated for the claims.

[ ] fewer than the inventors previously designated and a statement accompanies this request for the deletion of the name or names of the person or persons who are not inventors of the invention now being claimed.

[ ] a person not named previously as an inventor and a petition under 37 C.F.R. Section 1.48 is/has separately:
[ ] being filed
[ ] been filed

Respectfully submitted,

Dianne Rees

Date: April 2, 2003

Dianne M. Rees, Ph.D. (Reg. No. 45,281)
EDWARDS & ANGELL, LLP
P. O. Box 9169
Boston, MA 02209

Tel. No. (617) 439-4444
Fax. No. (617) 439-4170

Customer No. 21874

BOS2_331122.1

RCE/CPA 58118 (47992)

Express mail No. EL 945989385 US
Date of deposit of copy & filing 4/2/03:

April 16, 2003

COPY

Mailing Date: 4/2/2003
Client: 47992
Inventors: Samelson, et al.
Serial No.: 09/597,920
Filing Date: 6/19/2000

Attorney/Sec: WJD/hmt
~~Docket~~ No.: 58118 ~~CPA~~ RCE DMR 4/16/03

Patent No.:
Grant Date:

The dating stamp of the Patent and Trademark Office hereon will be taken as the date of filing of:

Request For Continued Examination (RCE)

Amendment and Remarks

Checks in the amount of $750.00 and $820.00

Express Mail Label No. EL 932685394 US

Express Mail No. EL 945987385 US
Date of Deposit & Copy of Filing: April 16, 2003

EDWARDS & ANGELL, LLP
COUNSELLORS AT LAW

Boston Main Account

NUMBER 710807

710807

COMMISSION Commissioner of Patents & Trademarks

Invoice No.	Invoice Date	Description	Invoice Amount	Discount	Payment Amount
47992.58118-03	04/01/2003	for PTO code 1253	$820.00	$0.00	$820.00

COPY

EXPRESS MAIL NO. EL945989385US
Date of [redacted] of Copy of 4/2/03 Filing:
April 2003

EDWARDS & ANGELL, LLP
COUNSELLORS AT LAW

Boston Main Account

NUMBER 710806

710806

COMMISSION Commissioner of Patents & Trademarks

nvoice No.	Invoice Date	Description	Invoice Amount	Discount	Payment Amount
17992.58118/03	04/01/2003	for PTO code 1001	$750.00	$0.00	$750.00

COPY

EXPRESS MAIL Label No. EL945989385US
Date of Deposit of Copy of 4/2/03 filing:
April 16, 2003

COPY

Express Mail Label No.: EL 932685394 US
Date of Deposit: April 2, 2003
Attorney Docket N . 58118 RCE (47992)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS	Samelson, et al.	EXAMINER:	Helms, Larry Ronald
U.S.S.N.:	09/597,920	GROUP:	1642
FILED:	June 19, 2000	Conf. No.	4586
FOR:	THE PROTEIN TYROSINE KINASE SUBSTRATE LAT AND ITS USE IN THE IDENTIFICATION OF (ANT)AGONISTS OF THE KINASE		

~~**BOX REISSUE**~~ BOX RCE DMR 4/16/03
Commissioner for Patents
Washington, D.C. 20231

AMENDMENT AND REMARKS

Sir:

This paper is responsive to the Final Office Action mailed August 8, 2003 and to the Advisory Actions mailed October 28, 2002 and March 7, 2003.

AMENDMENT

In the Specification

At page 10, after line 13, please **insert** the following:

--FIGURE 17 is a schematic diagram illustrating the role of LAT in linking the TCR to cellular activation.

FIGURE 18 is a schematic diagram showing the structure of the plasmid pEF BOS. The boxes indicate the SV40 origin, human EI-1α promoter region, the stuffer sequence from CDM8 and poly(A) adenylation site, respectively. The slashed areas in the EF-1α promoter region represent sequences from the first exon and part of the second exon, respectively. The lines flanking the boxes are sequences from pUC119. Major recognition sites for restriction

enzymes are shown.--

Please **delete** pages 37 and 60, and renumber the remaining pages as appropriate.

In the Claims

Please **cancel** claims **4-6, 29, 33 and 37-60** without prejudice.

Please **add** claims **61-84**.

61. (New) A purified antibody which is generated against a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 and which specifically binds to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4, but which does not cross-react with non-LAT ZAP 70 or non-LAT Syk substrates.

62. (New) The purified antibody of any of claims 61, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises the cytostolic tail of LAT.

63. (New) The purified antibody of any of claims 61, wherein said polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4 comprises amino acids 31-233 of LAT.

64. (New) The purified antibody of claim 61, wherein the at least a portion comprises SEQ ID NO:4.

65. (New) The purified antibody of any of claims 61-64, wherein the antibody is a polyclonal antibody.

66. (New) The purified antibody of any of claims 61-64, wherein the antibody is a monoclonal antibody.

67. (New) A purified antibody which is generated against a polypeptide comprising at least a portion of the amino acid sequence of SEQ ID NO: 4, wherein the at least a portion of the amino acid sequence comprises a phosphotyrosine residue and wherein the antibody specifically binds to a phosphorylated LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4, but which does not cross-react with other non-LAT ZAP 70 or non-LAT Syk substrates.

68. (New) The purified antibody of claim 67, wherein the at least a portion comprises at least about 5 amino acids of SEQ ID NO. 4.

69. (New) The purified antibody of claim 67, wherein the at least a portion comprises at least about 20 amino acids of SEQ ID NO. 4.

70. (New) The purified antibody of claim 67, wherein the at least a portion comprises SEQ ID NO. 4.

71. (New) The purified antibody of any of claims 67-70, wherein the antibody is a polyclonal antibody.

72. (New) The purified antibody of any of Claims 67-70, wherein the antibody is a monoclonal antibody.

73. (New) A purified antibody which is generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4 and which specifically binds to a LAT polypeptide comprising an amino acid sequence according to

SEQ ID NO: 4.

74. (New) The purified antibody of Claim 73, wherein the polypeptide comprising at least about five amino acids comprises at least about 20 amino acids of SEQ ID NO: 4.

75. (New) The purified antibody of Claim 73, wherein the polypeptide comprising at least about five amino acids comprises SEQ ID NO: 4.

76. (New) The purified antibody of Claim 74, wherein said polypeptide comprising at least about twenty amino acids of the amino acid sequence of SEQ ID NO: 4 comprises the cytostolic tail of LAT.

77. (New) The purified antibody of claim 76, wherein said polypeptide comprising at least about twenty amino acids of the amino acid sequence of SEQ ID NO: 4 comprises amino acids 31-233 of LAT.

78. (New) The purified antibody of any of claims 73-77, wherein the antibody is a polyclonal antibody.

79. (New) The purified antibody of any of claims 73-77, wherein the antibody is a monoclonal antibody.

80. (New) A purified antibody which is generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4, wherein the at least about five amino acids comprises a phosphotyrosine residue and wherein the antibody specifically binds to a phosphorylated LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4.

81. (New) The purified antibody of claim 80, wherein the polypeptide comprising at least

about five amino acids comprises at least about 20 amino acids of SEQ ID NO: 4.

82. (New) The purified antibody of claim 80, wherein the polypeptide comprising at least about five amino acids comprises SEQ ID NO: 4.

83. (New) The purified antibody of any of claims 80-82, wherein the antibody is a polyclonal antibody.

84. (New) The purified antibody of any of claims 80-82, wherein the antibody is a monoclonal antibody.

RESPONSE

Pending claims

Claims 4-6, 29, 33 and 37-60 are pending. Upon entry of this Amendment and Response, new claims 61-84 are presented for consideration.

Claims are canceled herein solely to expedite prosecution of the instant application and without prejudice to pursuing these claims in continuing and other related applications. No new matter is added by this amendment. Support for the newly added claims are found throughout the specification, in the claims as originally presented and in the Figures. In particular, attention is directed to the present application at page 38, page 41, lines 3-8, page 40, line 25 through page 41, line 1, and page 57, lines 5-7. Support for antibodies which do not cross-react with non-LAT ZAP 70 or non-LAT Syk substrates may be found at least at page 38, lines 9-12. Support for antibodies that are generated against a polypeptide of at least about 5 amino acids of the amino acid sequence of SEQ ID NO. 4 may be found at page 44, lines 6-9, for example. Support for antibodies directed against the cytostolic tail of LAT may be found at least at page 40, line 25 through page 41, line 1. Support for antibodies generated against polypeptides comprising amino

acids 31 to 233 of LAT may be found at least at page 57, lines 5-7. This sequence represents the sequence used as an immunogen to generate the antibodies disclosed in Applicants' Examples.

Applicants thank the Examiner for his helpful comments during the telephonic interview of October 24, 2002. The newly added claims provided with this filing are made to address the issues raised by the Examiner during the interview. It is believed that the new claims place the application in condition for allowance.

Objection to the Specification

The Examiner has objected to the Specification and states that "Schematic A" provided on page 37 should be removed and provided in the form of a Figure.

Applicants provided with their previous Amendment and Response to Final Rejection new Figures 17 and 18, to provide formal drawings corresponding to Schematic A and B respectively and have amended the Brief Description of the Drawings and the specification, as appropriate, to reflect this change.

Applicants thank the Examiner for approving the drawings submitted with Applicants' previous Response filed October 8, 2002, as indicated by the Advisory Action mailed October 28, 2002. Applicants respectfully request entry of the amendments to the Specification to describe the newly added Figures.

Rejection of Claims 4, 6, 29 and 37 Under 35 U.S.C. § 102(b) (Buday)

Claims 4, 6, 29 and 37 are rejected under 35 U.S.C. § 102(b) as being anticipated by Buday, et al., *The Journal of Biological Chemistry* 269: 9019-9023, 1994 ("Buday").

The Examiner asserts that Buday teaches an antibody specific for phosphotyrosine which is a portion of SEQ ID NO. 4 and therefore that the antibody of Buday would bind to SEQ ID NO: 4.

Applicants respectfully traverse the rejection as it would be applied to the newly added claims. Newly added claims 61-69 recite antibodies that specifically bind to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4 and do not cross-react with non-LAT ZAP 70 or non-LAT Syk substrates. Claims 70-84 recite that the antibodies are generated against a polypeptide comprising at least about five amino acids of the amino acid sequence of SEQ ID NO: 4 and that specifically bind to a LAT polypeptide comprising an amino acid sequence according to SEQ ID NO: 4.

Unlike the antibodies of the instant claims, Buday's antibody *would* cross react with non-LAT ZAP 70 or non-LAT Syk substrates, since it would react non-specifically with *any* polypeptides comprising a phosphotyrosine group. Therefore Buday neither teaches nor suggests the antibodies of claims 61-69.

With respect to claims 70-84, Buday's antibody is *not* generated against a portion of a LAT polypeptide comprising *at least about five amino acids of SEQ ID NO. 4.* This element of claims 70-84 must be given weight because the way in which the claimed antibodies are made *does* impact the structure and properties of the antibodies. The antigen-binding site of the claimed antibodies must recognize at least 5 amino acids of SEQ ID NO. 4 and must specifically bind to a LAT polypeptide according to SEQ ID NO. 4 (i.e., the full length LAT polypeptide). There is no teaching or suggestion of antibodies with these properties anywhere in Buday. To the extent Buday's antibody might arguably recognize a phosphorylated tyrosine in a phosphorylated LAT polypeptide, it does not recognize a sequence of at least 5 amino acids of a LAT polypeptide according to SEQ ID NO: 4 and therefore does not have the same binding specificity

required by claims 70-84.

Therefore, because Buday does not teach each element of the claims as required under 35 U.S.C. § 102, Buday does not anticipate the claims. See *In re Marshall*, 198 USPQ 344, 346 (CCPA 1978) ("[r]ejections under 35 U.S.C. §102 are proper only when the claimed subject matter is identically disclosed or described in the prior art.").

Applicants respectfully request that in view of the above arguments, the rejection should be reconsidered and withdrawn.

Rejection of Claims 4-5, 29 and 33 Under 35 U.S.C. § 102(e) (Hirth)

Claims 4-5, 29 and 33 stand rejected under 35 U.S.C. § 102(e) over Hirth, et al., U.S. Patent 5,058,959 ("Hirth"). The Examiner asserts that the antibody of Hirth is directed against a phosphotyrosine residue and as such, because the term "portion" reads on a single amino acid, Hirth allegedly anticipates the claims.

Applicants respectfully traverse the rejection as applied to the amended and newly added claims. As discussed above, as amended, claims 61-69 require that the antibodies recognize and *specifically* bind to a LAT polypeptide according to SEQ ID NO: 4 (i.e., a full length LAT polypeptide) and must *not cross react* with non-LAT ZAP 70 or non-LAT Syk substrates (i.e., non-LAT polypeptides which are phosphorylated by ZAP 70 and/or Syk). Hirth's antibodies would non-specifically cross-react with any polypeptides comprising a phosphotyrosine, including non-LAT ZAP 70 or non-LAT Syk substrates. Additionally, Hirth neither teaches nor suggests antibodies which recognize and specifically bind to a full length LAT polypeptide according to SEQ ID NO: 4 and which are generated against a polypeptide which comprises at least about 5 amino acids of SEQ ID NO. 4 as claimed in claims 70-84. Hirth nowhere teaches or suggests antibodies with these properties.

Therefore, in view of the above arguments, Applicants respectfully request that the rejection be reconsidered and withdrawn.

Rejection of Claim 38 Under 35 U.S.C. § 112, First Paragraph

Claim 38 is rejected under 35 U.S.C.§ 112, first paragraph. The Office Action expressly acknowledges that the specification is enabling for an antibody that binds a portion of SEQ ID NO:4. However, the position is taken that the specification does not reasonably enable an antibody that binds to "just any 20 amino acids" of SEQ ID NO:4 because antibodies generated against 20 amino acid fragments would not recognize the folded protein and as such would not be useful in detection. The Examiner concludes that it would require undue experimentation to use the claimed invention.

Applicants respectfully submit the rejection is moot in view of the cancellation of claim 38 and traverse the rejection to the extent it would be applied against any of the newly added claims. Antibodies are routinely generated against protein fragments and are routinely used in assays which do not rely on detecting tertiary conformations of proteins. For example, it was standard in the art at the time of filing (and still is) to perform Western blots of proteins electrophoresed on polyacrylamide gels comprising 10% SDS. In such gels, the proteins are denatured and do not retain the tertiary structure of the native protein. Yet Western blots have undeniable utility in assays which rely on the detection of specific proteins (e.g., such as in diagnostic assays). Additionally, antibodies generated against LAT peptides are also able to recognize non-denatured proteins in Flow Cytometry Assays as well as in immunohistochemistry assays. Accordingly, Applicants respectfully submit that the rejection of claim 38 is improper and should be reconsidered and withdrawn.

Rejection of Claims 39-44 Under 35 U.S.C. § 112, First Paragraph

Claims 39-44 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s) , at the time the application was filed, had possession of the claimed invention. The Examiner specifically objects to claims which recite "wherein SEQ ID NO: 4 comprises a carboxy-terminus and an amino-terminus, wherein said portion comprises at least 20 amino acids from" either the amino-terminus or carboxy-terminus. The Examiner asserts that "there is no support for antibodies that bind to at least 20 amino acids from the amino-terminal or carboxy-terminal."

Applicants respectfully submit that the rejection is moot in view of the cancellation of claim 39 and the fact that none of the newly added claims contain this language. Claim 39 has been cancelled solely to expedite the prosecution of the instant application as Applicants respectfully submit that specification clearly states at page 40 that that the present invention is not limited to specific portions of LAT for the generation of antibodies. As such, newly added claim 61 includes antibodies which recognize both N- and C-termini, as well as internal fragments of LAT and mutant forms of LAT.

In view of the above amendments and arguments, Applicants respectfully request that the rejection be reconsidered and withdrawn.

CONCLUSION

Applicants submit that the claims are allowable and that the Application is now in condition for allowance. Applicants respectfully request early favorable action by the Examiner.

If the Examiner believes that a telephone conversation with Applicants' agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned agent of record.

April 2, 2003

By: Dianne Rees

Dianne M. Rees, Ph.D. (Reg. 45,281)
EDWARDS & ANGELL, LLP
PO BOX 9169
Boston, Massachusetts 02209
(617) 951-3351

Customer No: 21,874